A CROSS SECTIONAL STUDY
ON THE PREVALENCE OF METABOLIC SYNDROME
IN PATIENTS ON ANTIPSYCHOTIC MEDICATION

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CERTIFICATE

I hereby declare that this dissertation titled ‘A Cross Sectional Study On The Prevalence Of Metabolic Syndrome In patients On Antipsychotic medication’ is a bonafide work done by Dr.Ranjith P at the Department of Psychiatry, Christian Medical College, Vellore. This work has not been submitted to any university in part or full.

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CERTIFICATE

I hereby declare that this dissertation titled “A CROSS SECTIONAL STUDY ON THE PREVALENCE OF METABOLIC SYNDROME IN PATIENTS ON ANTIPSYCHOTIC MEDICATION” is a bonafide work done by Dr.Ranjith P under my guidance at the Department of Psychiatry, Christian medical college, Vellore. This work has not been submitted to any university in part or full

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DECLARATION

I hereby declare that this dissertation titled "A CROSS SECTIONAL STUDY ON THE PREVALENCE OF METABOLIC SYNDROME IN PATIENTS ON ANTIPSYCHOTIC MEDICATION" is a bonafide work done by me under the guidance of Dr.Deepa Braganza, Professor of Psychiatry, Christian Medical College, Vellore. This work has not been submitted to any university in part or full.

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ABSTRACT

A CROSS SECTIONAL STUDY ON THE PREVALENCE OF METABOLIC SYNDROME IN PATIENTS ON ANTIPSYCHOTIC MEDICATION.

DEPARTMENT : PSYCHIATRY

NAME OF THE CANDIDATE : Dr.RANJITH P

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OBJECTIVES:

1.To study the prevalence of metabolic syndrome (MetS) as defined by the National Cholesterol Education Program's Adult Treatment Panel III(NCEP ATP III) criteria and the International Diabetic Federation(IDF) criteria, in patients receiving antipsychotic medication.

2. To assess the possible factors associated with metabolic syndrome in patients meeting the criteria for metabolic syndrome.

METHODS:

A cross sectional study was done to measure the prevalence of metabolic syndrome in patients using antipsychotic medication. Participants, fulfilling the inclusion and exclusion criteria, were recruited from the outpatient facility in the department of Psychiatry, Christian Medical College, Vellore, after obtaining written informed consent. Socio demographic data, anthropometric variables, fasting blood glucose, HDL cholesterol and serum triglyceride values were measured. Prevalence of metabolic syndrome was calculated using IDF and NCEP ATP III criteria.

RESULTS:

Prevalence of metabolic syndrome was found to be 23%(IDF) and 26%(NCEP). Prevalence was 20% in males and 36% in females, with no significant statistical difference (pvalue=0.167).The prevalence of metabolic syndrome was higher in patients receiving antipsychotic medication for more than 1 year (p value= 0.311) and in patients having more than one year duration of illness (p value= 0.481). The individual components of metabolic syndrome also had a higher prevalence in females, however the differences were not statistically significant except abnormality in HDL cholesterol(p value 0.01).

Introduction

Metabolic syndrome is a constellation of risk factors that when present in an individual, increases the risk for stroke, coronary artery disease and type2 diabetes mellitus. Metabolic syndrome constitutes central obesity, elevated cholesterol and triglycerides, impaired glucose tolerance and high blood pressure. Presence of metabolic syndrome in an individual leads to increased morbidity and mortality.

Patients with schizophrenia and other mental illnesses are especially prone to develop metabolic syndrome, due to their life style factors, genetic predisposition and due to antipsychotic medication. The role of antipsychotic medication in producing metabolic syndrome in a patient is of major interest to clinicians these days, particularly in the context of the shift of use of second generation antipsychotics as first line medication in psychosis.

There are various risk factors for the development of metabolic syndrome in people. They include poor diet habits, lifestyle factors, smoking and alcohol use, diabetes, chronic illnesses and genetic vulnerability. Prevalence of metabolic syndrome is high in people who have first degree relatives having diabetes mellitus or dyslipidemia.

Prevention is an important part of the management of metabolic syndrome as it helps to reduce the risk of severe cardiovascular morbidity and

other metabolic abnormality. Weight reduction, physical exercises are the key strategies to reduce the risk of metabolic syndrome. Pharmacological interventions are used only when the above strategies fail, and may not play a significant role.

Almost a quarter of the world population is estimated to have metabolic syndrome and is prone to complications related to it. Studies have shown that the prevalence of metabolic syndrome is higher in patients taking antipsychotic medications compared to the general population.

In this study we set out to measure the prevalence of metabolic syndrome in a sub group of patients attending a psychiatric tertiary care centre, and to look at the possible factors that are associated with, and which might predict development of metabolic syndrome in patients on antipsychotic medication.

Review Of Literature

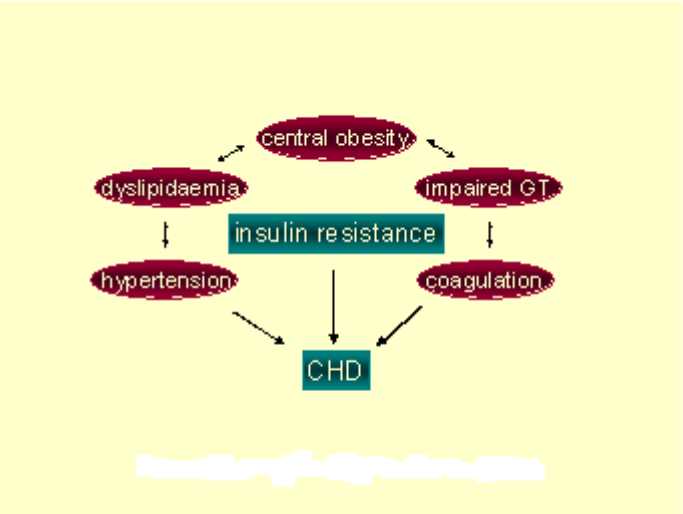
Metabolic syndrome

Metabolic syndrome is a group of conditions - increased blood pressure, elevated blood sugars, deranged cholesterol and accumulation of excess fat around the waist and abdomen, that when present together, can increase the chance of having heart disease, stroke and diabetes mellitus, thus increasing morbidity and mortality. These factors can present in a person in varying levels.

Metabolic syndrome also has various other names like syndrome X, Reavens syndrome, cardio-metabolic syndrome and insulin resistance syndrome. Metabolic syndrome has emerged as a major factor causing morbidity and mortality in this age of non-communicable diseases. Life style factors, nutrition and genetic vulnerability all contribute the development of this dreaded complication.

The term metabolic syndrome was first used by Hanefield and Leonardt in 1981. Reaven in 1988 proposed the name syndrome X to denote a group of conditions like hyperinsulinemia, glucose intolerance, and elevated cholesterol which were important in causing coronary artery disease. The term “deadly quartet” was used by Kaplan for the association of hypertension, obesity, glucose intolerance and hypertriglyceremeia in which hyperinsulinemia has a pathogenic association(1).

Components of metabolic syndrome



CHD- Coronary heart disease

PATHOPHYSIOLOGY

Insulin resistance

Insulin, secreted by the pancreas is a very potent anabolic hormone. It has effects on metabolism of lipid and protein, has a role in amino acid and ion transport, and affects cell cycle and cell differentiation(2). Insulin resistance is believed to be the major underlying pathophysiology for the development of metabolic syndrome. This is caused by the inability of the target organs to effectively utilize insulin, with a resultant hyperinsulinemia (3). This hyperinsulinemia may help to compensate some of the functions of insulin like maintaining normoglycemia, but causes over expression of insulin action in some

tissues. This overactivity of insulin in some tissues associated with insulin resistance in some tissues leads to the development of metabolic syndrome(4). There are several mechanisms proposed for the insulin resistance which include receptor, pre receptor and post receptor mechanisms.

Non esterified fatty acids are also believed to have role in the development of insulin resistance. Adipose tissue deposits in abdomen releases non esterified fatty acids into the blood stream. This in turn gets overloaded in the liver and muscles thereby leading to insulin over activity and resistance in these tissues. Lipoprotein lipase is an enzyme which breaks down lipoproteins to release free fatty acids. The action of lipoprotein lipase is stimulated by insulin. Insulin also inhibits lipolysis in adipose tissue. When insulin resistance develops, the inhibitory effect of insulin to lipolysis of adiposites reduces and more free fatty acids are produced. These free fatty acids in turn cause production of toxic materials inside the cells, further increasing the insulin resistance. This vicious cycle results more and more lipolysis and insulin resistance (5).

Role of obesity

The worldwide obesity epidemic has a major role in the increase in the prevalence of metabolic syndrome (6). Recent studies have shown that the central obesity appears before the onset of other metabolic syndrome factors and that weight reduction in the initial stages has an important role in the prevention of metabolic syndrome (7). Adipose tissue acts, not merely as a storage site for triglycerides. Recently it has been shown that it has other complex roles like secretion of adipokines. And these adipokines are reported to significantly

contribute to the development of metabolic syndrome (8). High levels of free fatty acids in the blood leads to accumulation of the same in liver thereby causing fatty liver.(9)

Hypertension

All the elements of metabolic syndrome, including insulin resistance, obesity, and dyslipidemia, likely have a role in the pathogenesis of hypertension. However obesity is believed to play a major role in the pathogenesis of metabolic syndrome(10). The Framingham Heart Study has shown that hypertension may be due to excess body fat and that it is so in 78% of men and 65% of women with hypertension. Increased retention of sodium is believed to be another causative factor in the development of hypertension in metabolic syndrome. Increased sodium retention by the kidneys, results in increased fluid volume, which causes hypertension.

Dyslipidemia

Elevation of triglycerides and lower level of HDL cholesterol are the major findings in metabolic syndrome. Insulin resistance and hyperinsulinemia leads to conversion of free fatty acids to triglycerides.

Low HDL is always an accompaniment of obesity. High triglycerides are a major cause for decreased HDL cholesterol. An increase in triglycerides, through various mechanisms, causes a reduction in the size of HDL particles, which are more readily metabolized. The smaller HDL particles are less effective in combating atherogenesis which, in turn, increases the risk of cardiovascular

diseases. Due to unknown mechanisms the level of HDL cholesterol is low in some individuals with normal level of triglyceride level.

In metabolic syndrome the level of LDL cholesterol is usually normal. However the existing LDL molecules are denser and smaller, which in turn is associated with atherogenesis.

Elevated LDL cholesterol also contributes to endothelial injury and resultant atherogenesis.

Inflammation

Chronic, subclinical inflammation is often seen associated with metabolic syndrome(5). Inflammatory mediators are seen to increase the risk of cardiovascular events and also believed to be one of the causes of insulin resistance. There are recent data to show that, obesity itself is a pro-inflammatory state. Inflammatory mediators like C-reactive protein, tumour necrosis factor alpha, Interleukin-6 and others are increasingly seen associated with obesity. A study on inflammatory mediators and inflammatory mediators revealed that C-reactive protein is strongly associated with obesity(11). Researchers also have argued the cause for including C- reactive protein as a criterion to diagnose metabolic syndrome due to its strong association with the problem (12).

Macrophages present in the adipose tissue can act as a source of pro-inflammatory markers.

Oxidative stress is believed to be the cause of inflammatory reaction in the adiposites(13).

Prothrombotic state

Prothrombotic state is also not included in the current definitions of metabolic syndrome despite its significant association with obesity and insulin resistance. People with metabolic syndrome have very high levels of plasma plasminogen activator inhibitor, which shows a dysfunctional fibrinolytic activity(14). Elevated levels of fibrinogen are also seen in metabolic syndrome.

Definitions and Diagnosis

Currently, there are several definitions to diagnose metabolic syndrome. Among them, those of the WHO, the International Diabetes Federation(15) and the revised National Cholesterol Education Program are the widely used definitions.

World Health Organisation (WHO)

The World Health Organisation attempted to standardise the criteria in 1988. Insulin resistance was viewed as a must have component to diagnose metabolic syndrome. To diagnose metabolic syndrome, insulin resistance was identified by the criteria given below. In addition, two other risk factors, listed below, were required.

Insulin resistance, identified by one of the following:

- Type 2 diabetes
- Impaired fasting glucose
- Impaired glucose tolerance
- or for those with normal fasting glucose levels (<6.1 mmol/L), glucose uptake below the lowest quartile for the background population under investigation under hyperinsulinemic, euglycemic conditions

Plus any two of the following:

- Antihypertensive medication and/or high blood pressure (≥140 mm Hg systolic or ≥90 mm Hg diastolic)
- Plasma triglycerides ≥1.7 mmol/L
- HDL cholesterol <0.9 mmol/L in men or <1.0 mmol/L in women
- BMI >30 kg/m^2 and/or waist:hip ratio >0.9 in men, >0.85 in women
- Urinary albumin excretion rate ≥20 μg/min or albumin:creatinine ratio ≥3.4 mg/mmol

One disadvantage of the above criteria is that special testing of blood glucose other than the routine clinical assessment may be required to diagnose metabolic syndrome.

European Group for the Study of Insulin Resistance (EGIR)

The European Group for the Study of Insulin Resistance (1999) stated that it is difficult to measure insulin resistance in diabetic patients, while fasting insulin values were considered as a reliable measure of insulin resistance in non diabetic patients. The EGIR recommended that metabolic syndrome can be diagnosed by top 25% of the fasting insulin values among non-diabetic individuals and two or more of the following:

- Hypertension: blood pressure ≥ 140/90 mmHg or antihypertensive medication
- Fasting plasma glucose ≥ 6.1 mmol/L
- Central obesity: waist circumference ≥ 94 cm (male), ≥ 80 cm (female)

- Dyslipidemia: TG ≥ 2.0 mmol/L and/or HDL-C < 1.0 mmol/L or treated for dyslipidemia

National Cholesterol Education Program Adult Treatment Panel III (2001) (NCEP)

The NCEP ATPIII introduced the concept and diagnostic guidelines for metabolic syndrome in 2001. It diagnoses metabolic syndrome in an individual if 3 or more of the following 5 are present.

- Blood pressure equal to or higher than 130/85 mmHg
- Fasting blood sugar (glucose) equal to or higher than 110 mg/dL
- Large waist circumference (length around the waist):
    - Men - 102 cm or more
    - Women – 88 cm or more
- Low HDL cholesterol:
    - Men - under 40 mg/dL
    - Women - under 50 mg/dL
- Triglycerides equal to or higher than 150 mg/dL

The advantage of the NCEP ATPIII criteria is that it is more user friendly and it gives both epidemiologists and clinicians valid, reliable and simple criteria to be used both in clinical and research settings.

International Diabetes Federation (IDF)

The International Diabetes Federation introduced the concept of metabolic syndrome and its criteria in 2006. IDF places more importance on the abdominal obesity as the other features of metabolic syndrome, including insulin resistance, are indirectly linked to the abdominal obesity. IDF also introduced ethnic specific values for the diagnosis of metabolic syndrome.

According to IDF metabolic syndrome is diagnosed if somebody is having Central obesity (defined as waist circumference with ethnicity-specific values - ≥94 cm for Europoid men and ≥ 80 cm for Europoid women, ≥ 90 cm for men and ≥ 80 cm for women for those of south and south east Asian , Japanese and ethnic south and central American origins)

And any two of the following:

- Raised triglycerides - > 150 mg/dL (1.7 mmol/L), or specific treatment for this lipid abnormality
- Reduced HDL cholesterol- < 40 mg/dL (1.03 mmol/L) in males, < 50 mg/dL (1.29 mmol/L) in females, or specific treatment for this lipid abnormality
- Raised blood pressure (BP) -systolic BP > 130 or diastolic BP >85 mm Hg, or treatment of previously diagnosed hypertension
- Raised fasting plasma glucose (FPG) - >100 mg/dL (5.6 mmol/L), or previously diagnosed type 2 diabetes
- If FPG is >5.6 mmol/L or 100 mg/dL, an oral glucose tolerance test is strongly recommended, but is not necessary to define presence of the

syndrome.

If BMI is >30 kg/m², central obesity can be assumed and waist circumference does not need to be measured.

All the four above mentioned criteria defining the metabolic syndrome using different criteria are more or less similar conceptually though there are some striking disparities. One major criticism of the WHO criteria is that it has included type2 diabetes as a criterion rather than reserving the diagnosis of metabolic syndrome to those who are at risk of developing diabetes mellitus. Also, impaired glucose tolerance measured by oral glucose tolerance test is consider to be impractical and leading to more costs, without much of an added benefit in predicting cardiovascular risk.

The NCEP criteria are criticized for the same reason as WHO criteria for including diabetes in the criteria. Also, it fails to identify those on treatment for hypertension or dyslipidemia when defining the criteria.

The strength of IDF is that it provides pragmatic waist circumference with ethnic specific values as a criterion. It also considers treatment for hypertension and dyslipidemia as criteria. However, like other systems mentioned above, IDF also fails to exclude diabetes as a criterion.

Considering the above pitfalls with the definitions, Resin and Alpert in 2005 proposed a better definition for metabolic syndrome which takes into account the major differences among the existing definitions. They proposed abdominal obesity as a major component based on its consistent association with metabolic

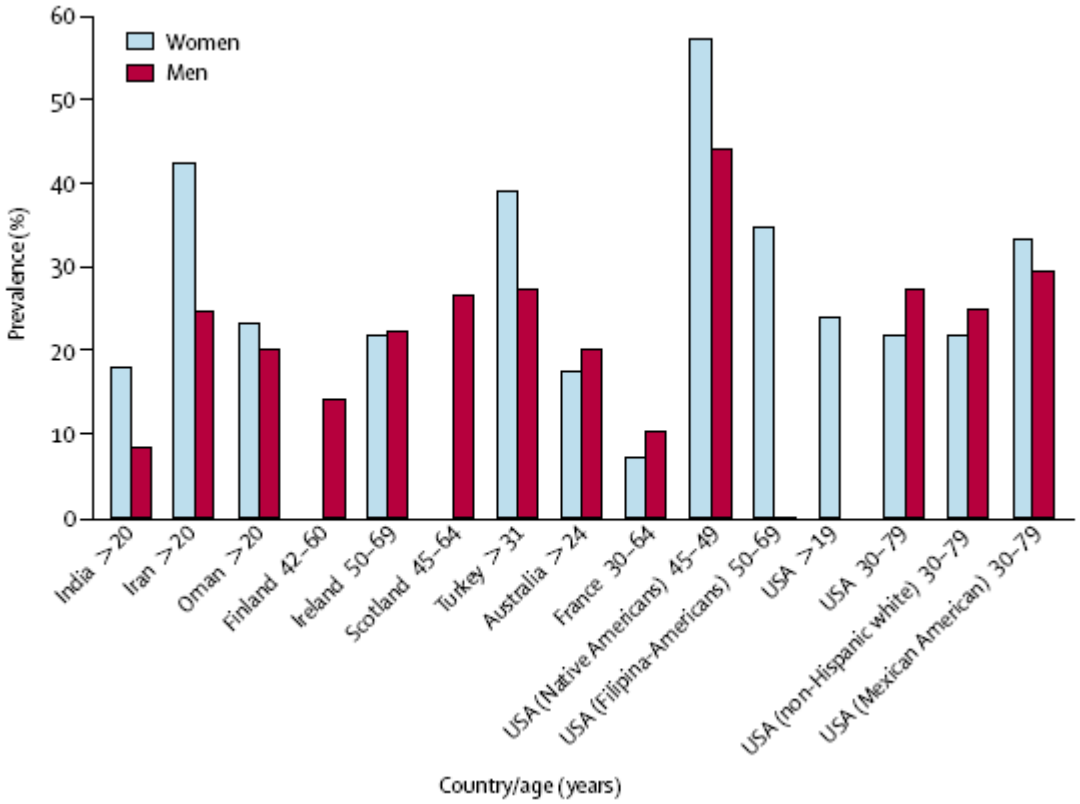
syndrome parameters. They also included ethnic specific cut off for waist circumference as defined by IDF. Previous diagnosis of dyslipidemia and hypertension also found place in the definition. They proposed a lower level of 100mg/dl for the fasting glucose value as recommended by the American Diabetes association. They also recommend including the WHO microalbuminuria criteria considering the fact that it predicts the development of chronic kidney disease.

Prevalence of metabolic syndrome in general population

A study has shown that the prevalence of metabolic syndrome varies from 8% in India to 24% in United States of America(5). The prevalence among women varies from as low as 7% in France to as high as 43% in Iran(5). A study in China has shown the prevalence of metabolic syndrome was higher in women compared to men in all age groups. There is age related increase in the prevalence of metabolic syndrome in United States in both men and women.

A recent assessment by the International Diabetic federation has found that the one quarter of world's population has metabolic syndrome and is prone to risk of cardio metabolic morbidity. Studies have shown variation in the prevalence of metabolic syndrome in different races and ethnic groups and among men and women(16)

World-wide prevalence of metabolic syndrome -Cameroon et al (17)



Prevention and treatment

The prevalence of metabolic syndrome is very high in the general population. At least a quarter of the world population has metabolic syndrome. Prevention of development of metabolic syndrome should be a priority in clinical practice. Identifying the risk factors of metabolic syndrome is an important direction in prevention of its development and complications(18). The treatment strategies include weight loss, lifestyle changes, diet modifications and appropriate use of pharmacological agents (19).

Educational intervention should be patient centered and should be focused on eliciting patient views on the knowledge of metabolic syndrome and the role of exercise and diet in reducing this complication. Clinicians and educators should be able to provide patients with short term or long term goals and address the barriers to change. Pharmacological strategies should be considered only if the non pharmacological strategies fail to adequately contain the problem(19).

Several studies have repeatedly stressed the role of weight reduction. They have recommended a weight loss of at least 10% during the first 6 months to a year and to continue weight losing strategies until the BMI is less than 25 (9).
The pharmacological strategies to reduce weight include two main classes of drugs, suppressants of appetite and inhibitors of nutritional absorption. Sibutramine and phentermine derivatives, that when taken in the early morning, reduce the appetite in the afternoon and evening. The only nutrient absorption inhibitor currently available in the market is orlistat, which is found to prevent up

to 30% absorption of fat. It is recommended for use as a single agent at a time to reduce weight (20).

Weight loss programs are usually successful only if a regular exercise program is also added along with it. Additionally regular exercise independently reduces the risk factors for metabolic syndrome(5).

Mental illness and metabolic syndrome

The life expectancy of people with severe mental illnesses like schizophrenia, is lower than that of the general population(21–24). Their mortality is 2 to 3 times more than the general population, and the mortality gap is increasing in the recent decades (25). The risk of dying due to a cardiovascular disease is nearly twice in people with severe mental illness(22–26).

Knowledge regarding the alarming nature of the physical comorbidity and mortality due to the same has led in recent decades to a rising concern about physical comorbidity in people with severe mental illness (27–29). In spite of significant somatic comorbidities, the access to quality health care is very poor for patients with severe mental illness(30).

The cardio metabolic risk factors are attributable to lifestyle, poor diet, and sedentary habits, in patients with severe mental illness. There is recent increase in awareness among clinicians regarding the role of antipsychotic agents in causing metabolic syndrome (27–29). And these metabolic changes are dependent on the dose of the antipsychotic drug (31) .

Table: Estimated prevalence and relative risk (RR) of modifiable cardiovascular disease risk factors in schizophrenia and bipolar disorder compared to the general population(32) .

	Estimated prevalence ,%(RR)	
Modifiable risk factors	Schizophrenia	Bipolar disorder
Obesity	45-55(1.5-2)	21-49(1-2)
Smoking	50-80(2-3)	54-68 (2-3)
Diabetes	10-15(2)	8-17(1.5-2)
Hypertension	19-58(2-3)	35-61(2-3)
Dyslipidaemia	25-69(≤5)	23-38(≤3)
Metabolic syndrome	37-63(2-3)	30-49(1.5-2)

In the general population, the presence of Metabolic syndrome is a strong predictor of Cardiovascular disease , mortality and diabetes mellitus (33) .

The concept of Metabolic syndrome is increasingly being recognised in psychiatric literature and this has helped in creating awareness among psychiatrist about the importance of assessing cardiovascular disease risk in patients being prescribed antipsychotics (34,35)

Table: Second generation antipsycotic agents and metabolic abnormalities

Antipsychotic	Weight gain	Risk for diabetes	Worsening lipid profile
Clozapine	+++	+	+
Olanzapine	+++	+	+
Risperidone	++	?	?
Quetiapine	++	?	?
Aripiprazole	±	No report	No report
Ziprasidone	±	No report	No report
Amisulpride	±	No report	No report

In the recent study, the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE), around one third of patients met NCEP criteria for metabolic syndrome at baseline(36,37). Among them 88% of patients with dyslipidaemia, 62% patients with hypertension and 38% of those with diabetes were not receiving treatment(37). There was significant difference between individual antipsychotic agents in causing adverse effects on weight, lipids, and glucose metabolism(37,38).

In a recent study comparing metabolic syndrome in patients diagnosed with schizophrenia in 2000-2006 to those who were diagnosed with schizophrenia in 1984-1995, second generation antipsychotic medication is implicated in causing twice as much of metabolic syndrome compared to first generation antipsychotic drugs(39).

While lifestyle factors, psychosis related factors and antipsychotic medication are commonly implicated as the causal factors of metabolic syndrome in schizophrenia, recent studies have explored the possible genetic causes for the metabolic syndrome in this sub group of patients (35, 36). Studies have shown that there is an increased liability for patients with schizophrenia for developing metabolic syndrome even without taking antipsychotic medication, as well as increased risk for developing diabetes mellitus in first degree relatives (42) There is also evidence for elevated blood sugar levels, visceral adiposity, and increased cortisol levels in patients before starting treatment with antipsychotic drugs(43,44). A higher vulnerability for developing metabolic syndrome in schizoaffective disorder compared to bipolar disorder and schizophrenia is shown in a recent study (45) .

Table: Prevalence of metabolic syndrome in people with schizophrenia

Study	Country	N	Mean age	%MetS
Heiskanen et al (78)	Finland	35	44.5	37.1
Almeras et al (62)	Canada	42	31.7	33.0
	Canada	45	28.4	11.0
Basu et al (65)	USA	33	44.5	42.4
Cohn et al (68)	Canada	240	42.7	44.6
Kato et al (80)	USA	48	40.3	63.0
Straker et al (96)	USA	89	39.8	29.2
Meyer et al (83)	USA	1231	42.8	35.8
McEvoy et al (82)	USA	342	39.8	40.9
		92	44.2	56.2
Saari et al (88)	Finland	31	31.0	19.4
Correll et al (69)	USA	367	42.9	37.3
De Hert et al (71)	Belgium	430	36.5	32.3

Table: Prevalence of metabolic syndrome in people with schizophrenia(contd)

Study	Country	N	Mean age	%MetS
Lamberti et al (81)	USA	93	34.4	53.8
Meyer et al (84)	USA	80	49	51.2
Bobes et al (66)	Spain	1452	40.7	24.6
Correll et al (70)	USA	294	43.6	34.3
De Hert et al (73)	Belgium	208	33.7	27.9
		23	33.7	13
		31	33.7	9.7
		25	33.7	56
		54	33.7	33.3
		25	33.7	32
		50	33.7	24
L'Italien et al (79)	USA	155	41.4	25.8
		267	40.7	19.9
		373	37.7	41.6
		380	37.6	27.9

Table: Prevalence of metabolic syndrome in people with schizophrenia (contd)

Study	Country	N	Mean age	%MetS
Mulder et al (85)	Netherlands	112	36	25
Sicras-Mainar et al	Spain	742	55.1	27
(94)		57	37.5	35
Srisurapanont et al	Thailand	38	53.7	36.2
(95)		44	44.3	31.8
Suvisaari et al (97)	Finland	108	34.6	34
Teixeira and Rocha	Brazil	122	23.1	5.7
(98)		122	26.8	13.1
Cerit et al (67)	Turkey	108	21.9	5.6

Table: Incidence of metabolic (MetS) in people with schizophrenia

Study	Country	N	Mean age	%MetS
De Hert et al (71)	Belgium	31	36.7	61.3
			36.7	29
Attux et al (64)	Brazil	44	26.3	6.8
De Hert et al (72)	Belgium	155	33.7	18.7
		16	33.7	6.3
		16	33.7	0
		20	33.7	45
		45	33.7	24.4
		21	33.7	19.1
		37	33.7	10.8
L'Italien et al (79)	USA	91	41.4	14.3
		151	40.7	5.3
		212	37.7	27.4
		198	37.6	15.7
Saddichha et al (89)	India	30	26.9	27.5
Srisurapanont et al (95)	Thailand	35	34.7	20

Study	Country	N	Mean age	%MetS
De Hert et al (74)	Belgium	122	26.8	9.8
		108	25.1	27.8
		8	25.1	12.5
		10	25.1	0
		12	25.1	50
		34	25.1	41.3
		24	25.1	12.6
		20	25.1	10.2
Meyer et al (84)	USA	164	40.9	34.8
			40.9	43.9
		147	40.9	30.6
			40.9	30.6
		143	40.9	37.8
			40.9	37.1
		77	40.9	37.7
			40.9	29.9
		129	40.9	37.2
			40.9	38

The propensity of antipsychotic drugs to induce weight gain is seen partly as the cause for metabolic syndrome. All antipsychotic drugs cause weight gain, however the propensity to cause clinically relevant weight gain(>7% increase) varies between different antipsychotic agents(46). Studies have shown a link between the receptor profile of antipsychotic agents and their ability to cause metabolic changes and weight gain. Some authors link the receptor profile of antipsychotics to their differential liability to induce weight gain and other metabolic changes (44,46). Effect on muscarinic receptors as an antagonist could lead to increased weight gain. Antagonistic effect on the dopamine reward system can lead to increased appetite and thus increased weight gain.(47).Studies have also shown the irreversibility of antipsychotic agents on weight gain even after discontinuation of antipsychotic drugs possibly due to a direct effect on pancreatic function(42,44,46).

Some recent studies show that children and adolescents are more prone to metabolic side effects and weight gain on antipsychotic medication when compared to adult subjects (48,49).

GUIDELINES FOR SCREENING AND MONITORING

Prevention of development of metabolic syndrome should be a priority while starting antipsychotic medication. In order to prevent this complication, diet modification and lifestyle interventions should be started along with the commencement of treatment with antipsychotics.

A failure to provide appropriate and effective general health care to mentally ill patients is due to a lack of consensus regarding the responsibility towards the patient. Usually, the general medical needs of the mentally ill are neglected and the psychiatrist's focus is mainly on the efficacy of antipsychotics on the psychotic symptoms.

Though there are many national and international guidelines for monitoring metabolic syndrome and other general health indicators, these are rarely used in the routine care of the patients(50–52).

Assessment of cardio metabolic risk profile is important before the commencement of treatment with antipsychotic drugs. The sensitivity of the combination of fasting glucose and waist circumference in identifying patients with metabolic syndrome, is as high as 100%. Before start of treatment, the cardio-metabolic risk profile of a patient should be assessed (53).

Lifestyle interventions, physical exercises, and diet modification should be started early to prevent complications(24). The lowering of risk while successfully instituting the above measures is very significant. A 30% reduction

in cardiovascular disease risk is seen upon reducing the cholesterol levels by 10%. A 6% lowering of blood pressure leads to a 15% reduction in the cardiovascular risk. Similarly a 50 to 70 % reduction in cardiovascular disease prevalence is seen with cessation of smoking. A 20 minutes brisk walk a day and keeping the body mass index below 25 helps to reduce the cardiovascular disease risk by 30 to 50% (24). There is growing evidence to support the effectiveness of lifestyle interventions to reduce the risk of cardiovascular and metabolic effects in mentally ill patients.

The role of regular physical activity in reducing the risk of metabolic side effects and cardiovascular disease risk is undisputed (54). Regular physical activity helps in the prevention of obesity, hypertension, dyslipidemia and diabetes (55,56). Therefore, regular physical exercise should be included in the lifestyle modification intervention in schizophrenia. Though there are no strict guidelines to recommend the type and duration of physical activity in patients with schizophrenia, 30 minutes walk at least 5 days a week will be sufficient to significantly reduce the metabolic risk. While selecting the physical activity attention should be given to the patient's personal preference and attitude towards physical activity (54,57).

Switching to a different antipsychotic drug that has reduced potential to cause metabolic side effects is an important strategy if a patient develops metabolic syndrome with a particular antipsychotic. Instituting appropriate measures to reduce blood pressure, control blood glucose or to lower cholesterol and triglycerides should be considered along with switching antipsychotic drug. While doing this, consultation with a specialist should be done if it is appropriate.

There is recent evidence to suggest that statins are effective and safe in patients with schizophrenia who are exposed to antipsychotics. However statins have little role in reversing the metabolic syndrome once it has developed (58,59).

AIMS AND OBJECTIVES

Primary Objective

To study the prevalence of metabolic syndrome (MetS) as defined by the National Cholesterol Education Program's Adult Treatment Panel III criteria and the International Diabetic Federation criteria, in patients receiving antipsychotic medication.

Secondary objective

To assess the possible factors associated with metabolic syndrome in patients meeting the criteria for metabolic syndrome.

METHODOLOGY

Setting:

The study was conducted in the Department of Psychiatry, Christian Medical College, Vellore. This is a 122 bedded tertiary care centre offering inpatient and outpatient treatment for patients with psychiatric illness. The hospital caters to patients from various parts of the country.

The facilities in the department include a well equipped outpatient department inpatient facility, nursing service, occupational therapy, pharmacy services,laboratory services and emergency services.

The outpatient department functions 6 days in a week and both new and review patients are seen. Emergency care is provided 24 hours in a day.

This institution has the facilities of a tertiary referral centre, but serves in addition as the nearest psychiatric centre for a radius of approximately 150 miles. The department has four units, two serving adult clients, one for children and adolescents, and one for rehabilitation services. Approximately 11000 new patients and 90000 review patients are seen in a year in this centre. On an average 1000 patients are provided inpatient treatment in an year.

Participants:

Participants for the study were recruited from the outpatient facility in the department of psychiatry. Patients attending the outpatient facility were screened using the inclusion and exclusion criteria. Patients who met these were given an information leaflet in their own language and given an explanation of the possible risks and benefits of the study. Those who gave written consent to be included in the study were recruited.

Inclusion Criteria:

- Age above 18 years
- On stable dose of antipsychotic drugs for the last 3 months or more

Exclusion Criteria:

- Patients with alcohol abuse or dependence or organic conditions
- History of diabetes or hypertension before starting antipsychotic drugs
- On other medications like mood stabilizers, which may have confounding effect on the outcome variable.

Variables:

The variables assessed included age, gender, individual metabolic parameters like waist circumference, fasting blood sugar, HDL cholesterol, triglycerides, duration of illness and duration of antipsychotic use.

Data Sources/measurement:

Patients attending the psychiatric OPD were screened. Those meeting the inclusion criteria were enrolled into the study after obtaining written informed consent.

Data collection was begun after approval by the Institutional review board. Data was collected from May 2012 to October 2012.

Demographic data including age, sex, occupational and marital status, family history of medical and mental illness were collected from the patient and the relative. Subsequently blood pressure, height, body weight and waist circumference were measured and documented. Patients were asked to do fasting blood glucose and fasting triglycerides, and HDL cholesterol during the next hospital visit. If the patients had done the blood tests (AC, HDL, Triglycerides) within last one month at the time of recruitment as part of their routine care, the same values were used for the study and blood tests were not repeated.

Prevalence of metabolic syndrome was assessed using NCEP ATPIII criteria and International Diabetic Federation criteria.

Sample size:

Sample size was calculated using a previous study which estimated the prevalence of metabolic syndrome as 32% (60). Sample size required to detect a prevalence of 32% with a 10% margin of error for 95% CI was 90. The following assumptions were made for the calculation of the sample size:

Prevalence	= 32%
Margin of error	= ±10
Confidence level	= 95%
Total required sample size	= 90

Quantitative variables:

Quantitative variables included waist circumference, blood glucose, HDL and triglyceride values, duration of illness and duration of antipsychotic use.

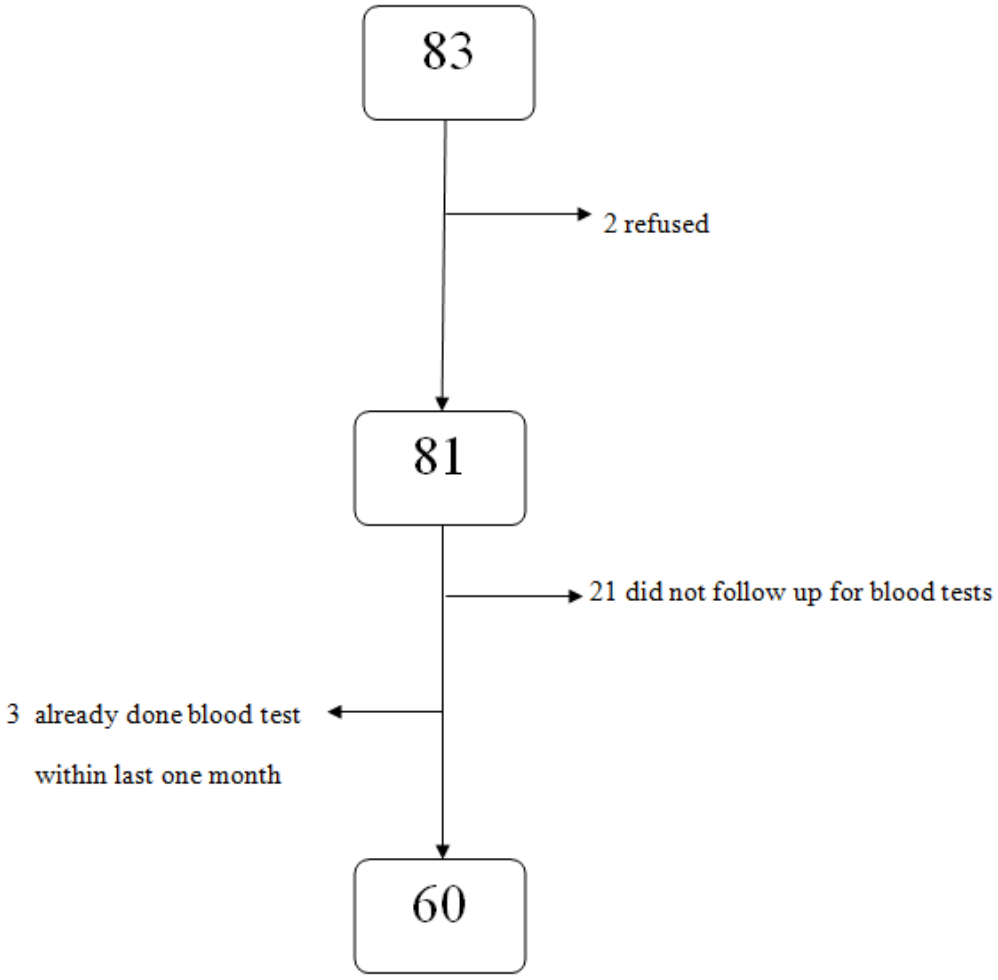
Statistical methods:

The statistical analysis was performed using Stata (SE 10.1 version). Results were expressed as mean ± standard deviation (SD). Pearson's chi-square test was applied to test the relationship of categorised independent and dependent variables.

RESULTS

A total of 83 patients were screened for the study. They were referred by colleagues based on the inclusion and exclusion criteria. 2 people declined consent as they were living far away from hospital and expressed inability to do blood tests at the hospital. A total of 81 patients were recruited into the study after obtaining written informed consent. 57 subjects followed up for giving fasting blood sample and 3 subjects had already done blood tests in the last one month. Hence the analysis and results are based on data for 60 participants.

Flow chart

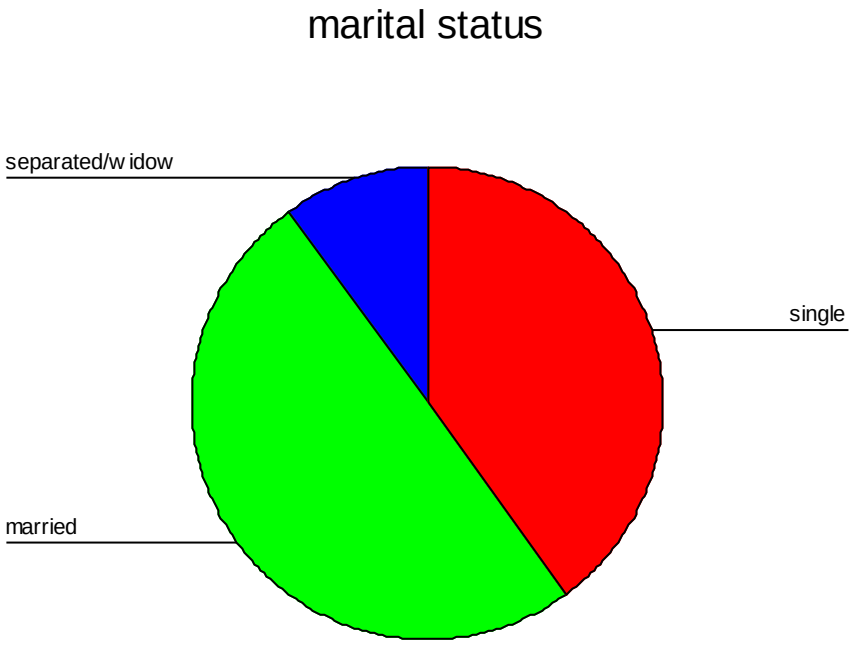


Out of the 60 subjects, 35 were male 25 were female. The mean age of the participants was 36 years. 19 subjects were illiterate, 30 had school education and 11 subjects had undergone graduate training.

Distribution of participants according to marital status

Marital status	Number of participants	percentage
Single	24	40
Married	30	50
Separated/widow	6	10
Total	60	100

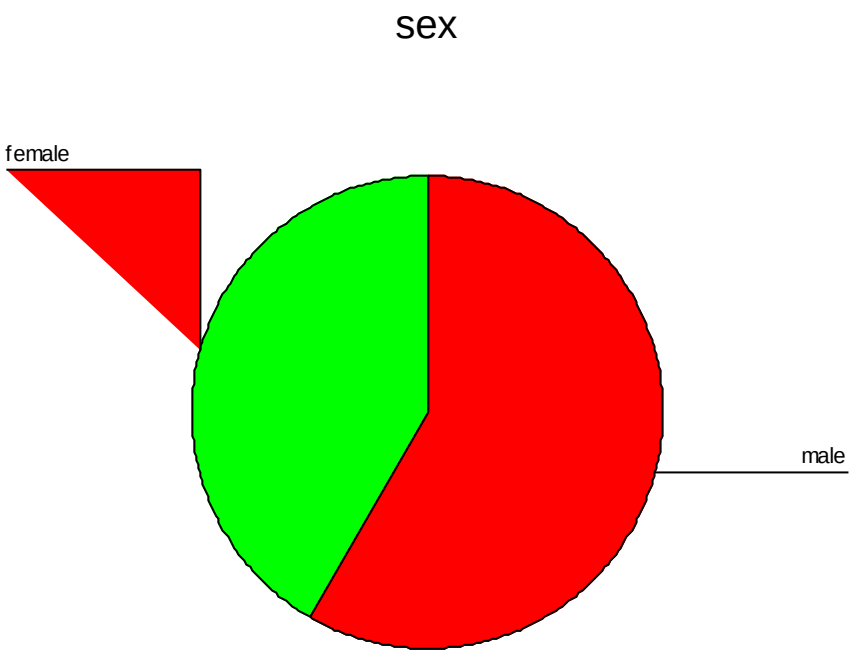
Out of 60, 24 subjects were unmarried-, 30 were married and 6 were either widowed or separated from the partner.



Distribution based on gender

Gender	No of participants	Percentage
Male	35	58
Female	25	42
Total	60	100

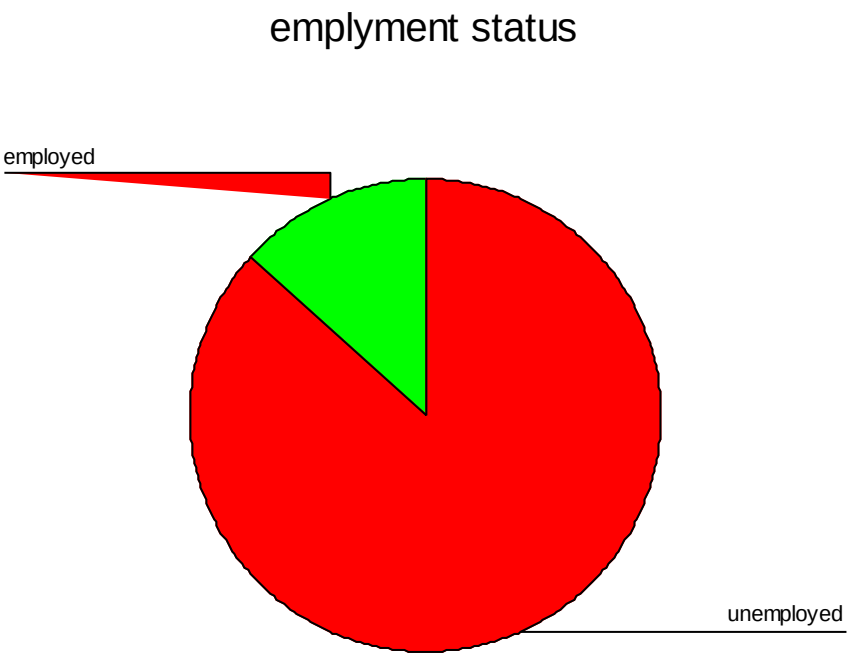
35 (58%) were male and 25(42%) were female.



Distribution based on employment status

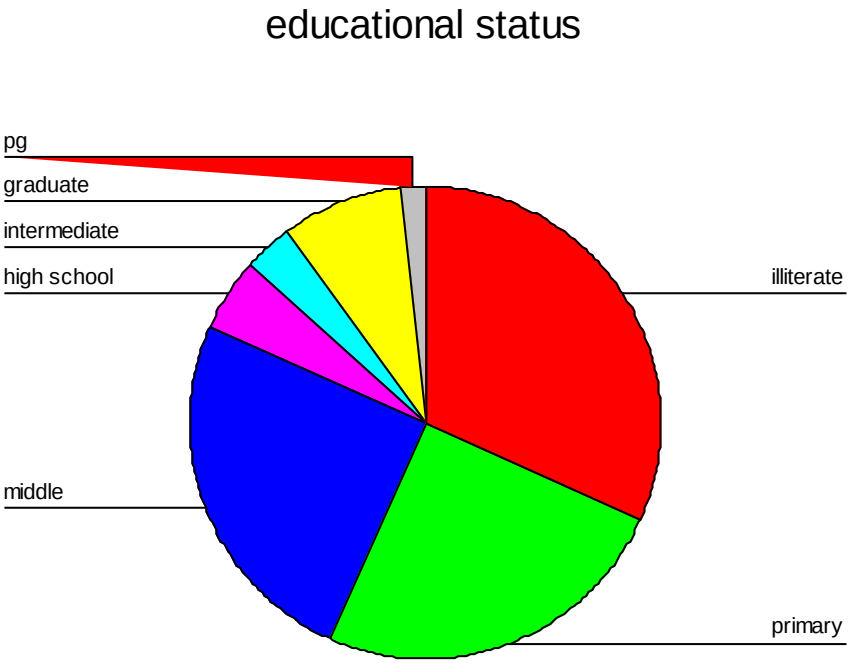
Employment Status	No of participants	Percentage
Unemployed	52	87
Employed	8	13
Total	60	100

52 (87%) were unemployed and 8(13%) were employed.



Distribution based on educational level

Educational status	Number of participants	Percentage
Illiterate	19	31
Primary	15	25
Middle school	15	25
High school	3	5
Intermediate	2	3.3
Graduate	5	8.3
Post graduate	1	1.7
Total	60	100


educational status
pg
graduate
intermediate
high school
illiterate
middle
primary

Distribution of means of variables

Variable	Mean	Standard Deviation	Minimum value	Maximum Value
Age	36 years	11	20	65
Waist circumference	87 cm	10	65	112
Blood pressure – systolic	119 mmHg	11	100	150
Blood pressure- diastolic	76 mmHg	6	70	90
Fasting blood sugar	92 mg/dL	15	71	185
HDL cholesterol	41mg/dL	10	26	73
Triglycerides	145 mg/dL	90	39	535

Distribution according to criteria satisfying metabolic syndrome definition.

In the tables listed below, each variable is shown depending on whether they satisfied the criteria for metabolic syndrome or not. The number of participants are divided according to this.

Distribution according to waist circumference

Waist Circumference (wc)	Number of participants(IDF)	Number of participants(NCEP ATP III)
MetS(wc)+	33 (55%)	18(30%)
MetS(wc)-	27(45%)	42(70%)
Total	60(100%)	60(100%)

MetS(wc)+ → Number of participants satisfying criteria for MetS

MetS(wc)- → Number of participants not satisfying the criteria

The mean value of weight circumference was 87 cm with a standard deviation of 10. Out of 60 subjects, 33 (55%) were above the specified value according to IDF and 18 (30%) met the criteria according to- NCEP ATP III.

Distribution according to fasting blood sugar

Fasting blood sugar (ac)	Number of participants(IDF)	Number of participants(NCEP ATP III)
MetS(ac)+	8(13%)	3(5%)
MetS(ac)-	52(87%)	57(95%)
Total	60(100%)	60(100%)

MetS(ac)+ → Number of participants satisfying criteria for MetS

MetS(ac)- → Number of participants do not satisfying the criteria

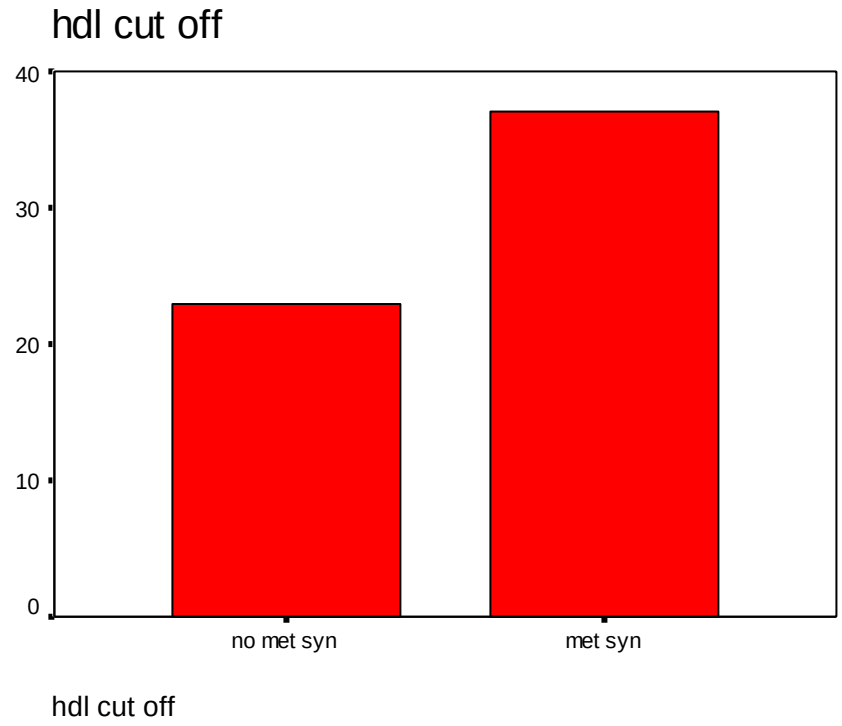
The mean value of fasting blood sugar was 92 with a standard deviation of 15. 8(13%) participants met the criteria according to IDF and 3(5%) met the criteria according to NCEP ATP III.

Distribution according to HDL Cholesterol

HDL Cholesterol (hdl)	Number of participants(IDF)	Number of participants(NCEP ATP III)
MetS(hdl)+	37(62%)	37(62%)
MetS(hdl)-	23(38%)	23(38%)
Total	60(100%)	60(100%0

MetS(hdl)+ → Number of participants satisfying criteria for MetS

MetS(hdl)- → Number of participants do not satisfying the criteria



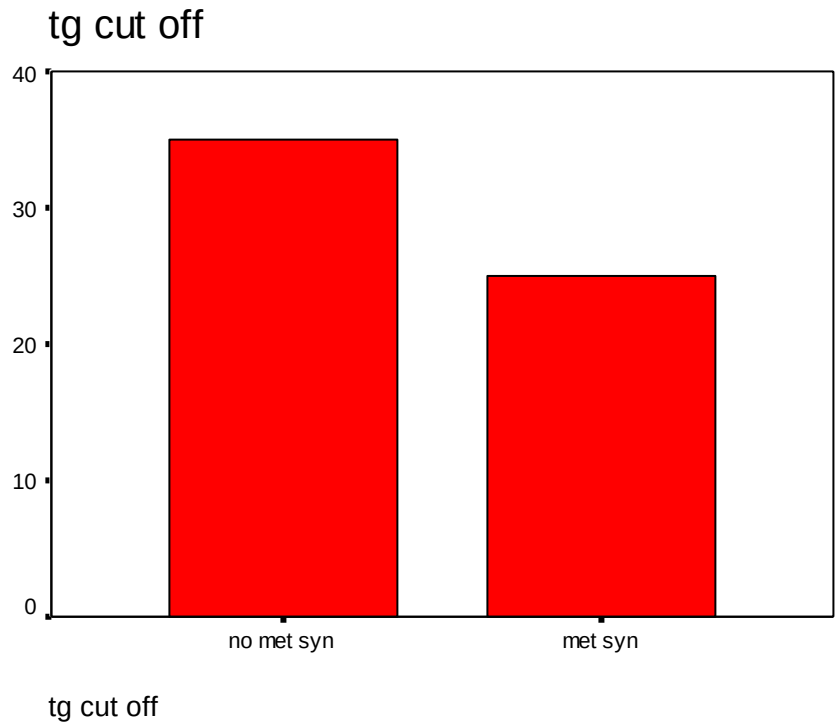
The mean value of HDL Cholesterol was 41mg/dL with a standard deviation of 10. Out of 60 subjects, 37 (62%) subjects met the criteria according to IDF and NCEP ATP III.

Distribution according to Triglyceride (tg) value.

Triglycerides (tg)	Number of participants(IDF)	Number of participants(NCEP ATP III)
MetS(tg)+	25 (42%)	25(42%)
MetS(tg)-	35(58%)	35(58%)
Total	60(100%)	60(100%)

MetS(tg)+ → Number of participants satisfying criteria for MetS

MetS(tg)- → Number of participants do not satisfying the criteria



The mean value of Triglycerides was 146 cm with a standard deviation of 90. Out of 60 subjects, 25(42%) were above the specified value according to IDF and NCEP ATP III.

Distribution according to blood pressure

Blood pressure (bp)	Number of participants(IDF)	Percentage (IDF)	Number of participants(NCEP ATP III)	Percentage (NCEP ATP III)
MetS(bp)+	15	25	15	25
MetS(bp)-	45	75	45	75
Total	60	100	60	100

MetS(bp)+ → Number of participants satisfying criteria for MetS

MetS(bp)- → Number of participants do not satisfying the criteria

The mean value of HDL Cholesterol was 41mg/dL with a standard deviation of 10. Out of 60 subjects, 37 (62%) subjects met the criteria according to IDF and NCEP ATP III.

Prevalence of metabolic syndrome.

Metabolic Syndrome (MetS)	Number of participants(IDF)	Number of participants(NCEP ATP III)
MetS+	**14 (23%)**	**16(27%)**
MetS-	46(77%)	44(73%)
Total	60(100%)	60(100%)

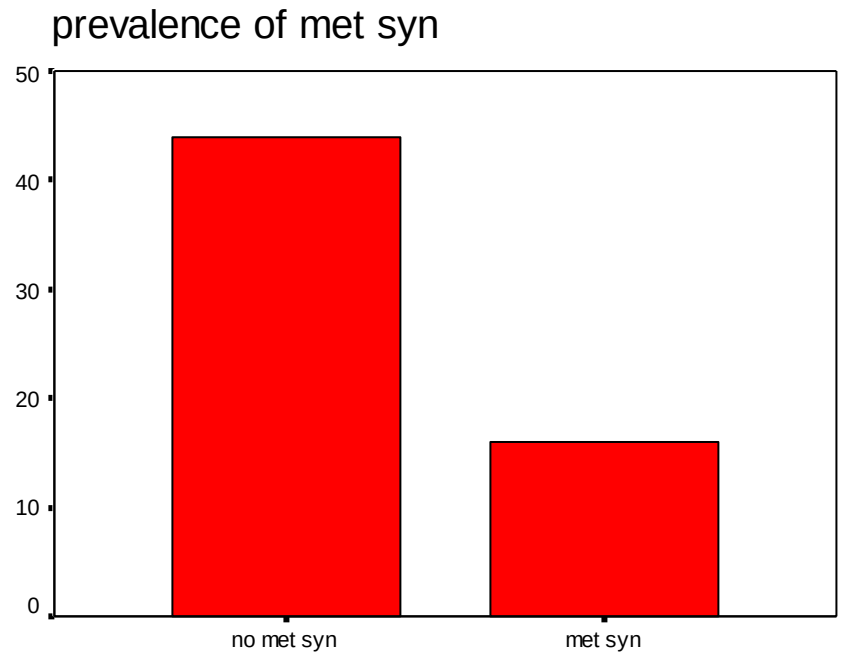
MetS + → Number of participants satisfying criteria for MetS

MetS - → Number of participants do not satisfying the criteria

The prevalence of metabolic syndrome calculated separately with International Diabetic Federation(IDF) criteria and US National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria

Prevalence of metabolic syndrome according to IDF = 14 (23%)

Prevalence of metabolic syndrome according to (NCEP ATP III) = 16 (27%)



prevalence of met syn

Gender wise distribution of metabolic syndrome

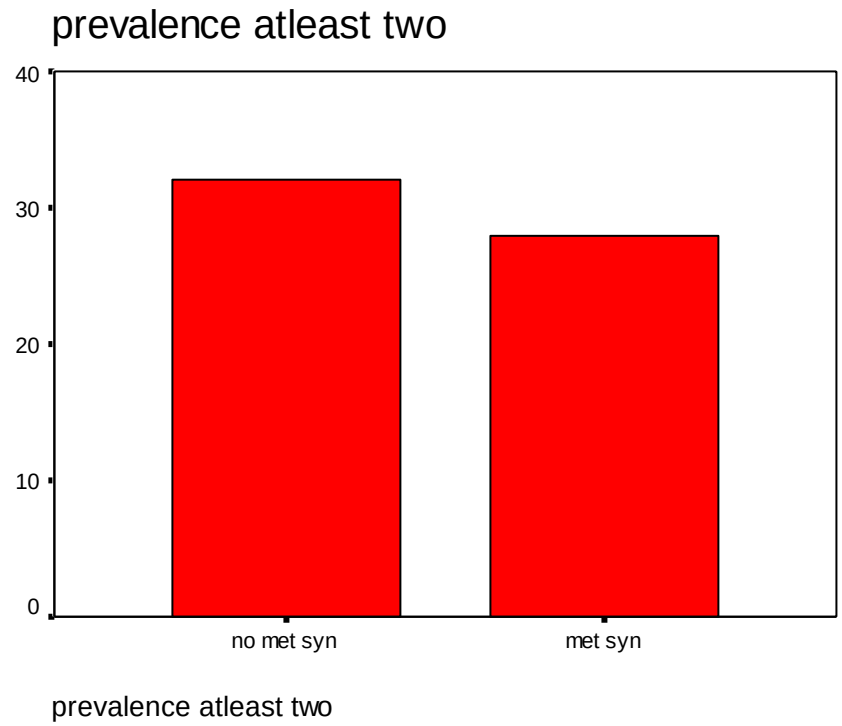
Metabolic Syndrome (MetS)	Number of participants(NCEP ATP III)	Percentage (NCEP ATP III)
MetS-male	7	20
MetS- female	9	36

Gender specific prevalence of metabolic syndrome was also found out using NCEP ATP III criteria. Prevalence of metabolic syndrome in was found to be **20%** in males and **36%** in females. Chisquare test was done to find the significance of difference. There was no difference between the two groups (p value of 0.167). It was inferred that the prevalence of metabolic syndrome was higher in females compared to males.

Prevalence based satisfying at least two criteria of metabolic syndrome according to NCEP ATP definition

The table below shows how many participants meet at least two criteria for metabolic syndrome. Though they may not satisfy the criteria for metabolic syndrome, the presence of the risk factors makes them vulnerable for cardiovascular and other morbidities associated with metabolic syndrome.

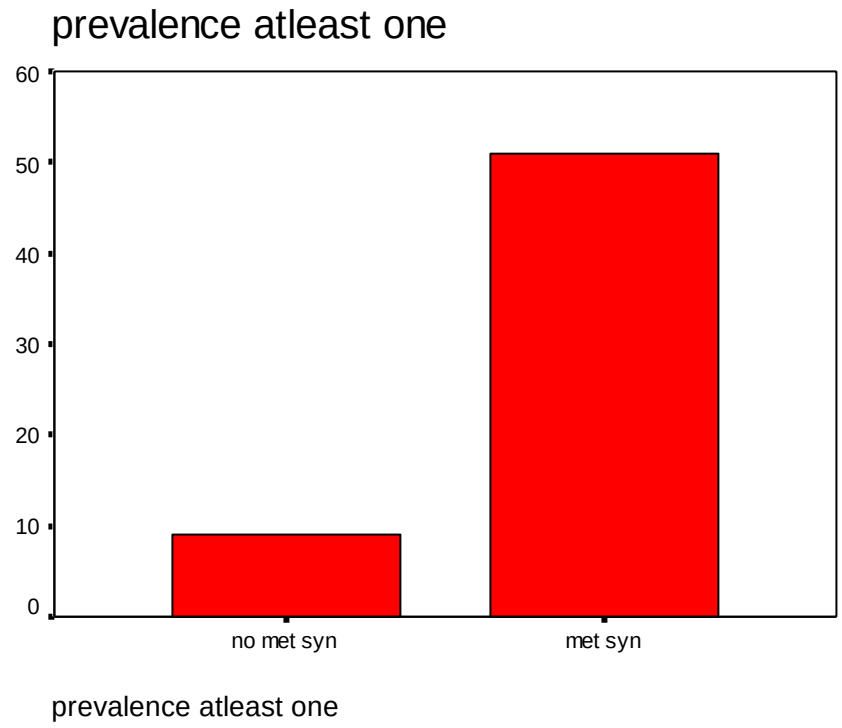
MetS(At least 2 crietria)	Participants	Percentage
MetS+	28	47
MetS-	32	53
Total	60	100



Presence of at least one criteria of NCEP ATP definition

51 out of 60 participants had at least one risk factor among the five.

MetS	Participants	Percentage
MetS+	51	85
MetS-	9	15
Total	60	100



Distribution of variables across genders

The distribution of various variables across gender was calculated. The mean and standard deviation, and a chisquare test were done to assess the difference between the groups.

Systolic Blood Pressure

Systolic BP	N	Mean	SD	F value	P value
Male	35	120	11.1	2.8	0.097
Female	25	116	11.5		

The mean value of systolic blood pressure was higher in males compared to females. The difference was not statistically significant.

Diastolic blood pressure

Diastolic BP	N	Mean	SD	F value	P value
Male	35	77	5.8	1.69	0.198
Female	25	75	6		

The mean value of diastolic blood pressure was higher in males compared to females. The difference was not statistically significant.

Fasting blood sugar

Fasting blood sugar	N	Mean	SD	F value	P value
Male	35	89	7.3	2.58	0.113
Female	25	96	21		

The mean value of fasting blood sugar was higher in females compared to males. The difference was not statistically significant.

HDL cholesterol

HDL cholesterol	N	Mean	SD	F value	P value
Male	35	38	6	11.6	**0.001**
Female	25	46	11.8		

The mean value of HDL cholesterol was higher in females compared to males. The difference was not statistically significant.

Triglyceride

TG	N	Mean	SD	F value	P value
Male	35	147.8	96	0.054	0.817
Female	25	142.3	81		

The mean value of triglycerides was higher in males compared to females. The difference was not statistically significant.

Waist circumference

Waist circumference	N	Mean	SD	F value	P value
Male	35	94	14	11.43	0.1
Female	25	82	22		

The mean value of waist circumference was higher in males compared to females. The difference was not statistically significant

Presence of at least two components of metabolic syndrome out of five – A gender- wise distribution

A gender wise distribution of criteria meeting at least two criteria of metabolic syndrome is calculated.

Gender	MetS(2 criteria)+	No MetS	Total
Male	15 (43%)	20 (57%)	35
Female	13(52%)	12(48%0	25
Total	32 (53%)	28 (47%)	60

The prevalence based on at least two components of metabolic syndrome was 43% in males and 52% in females. The difference was not statistically significant.

Prevalence of at least one component of metabolic syndrome out of 5 – A gender-wise distribution

Gender	MetS(1 criteria)+	No metS	Total
Male	29(82%)	6 (17%)	35
Female	22(88%)	3(12%)	25
Total	51(85%)	9(15%)	60

The prevalence based on at least one component of metabolic syndrome was 82% in males and 88% in females. The difference was not statistically significant.

Distribution according Duration of illness

The participants were divided into two groups; those who were ill for less than one year, and those with illness for more than one year.

Duration of Illness	MetS+ (NCEP ATP III)	MetS- (NCEP ATP III)	Total
Less than 1 year	2	9	11
More than 1 year	14	35	49
Total	16	44	60

Eleven subjects had had been ill for less than one year. Of these, two were found to have metabolic syndrome. 14 subjects out of 49, who had been ill for more than 1 year, met the criteria for metabolic syndrome. Chisquare test was done and no significant difference was found between the two groups(p value of 0.481).

Distribution according to Duration of antipsychotic use

We wished to see the effect of the duration of antipsychotic exposure on the prevalence of metabolic syndrome.

Duration of Antipsychotic use	MetS+ (NCEP ATP III)	MetS- (NCEP ATP III)	Total
Less than 1 year	6	23	29
More than 1 year	10	21	31
Total	16	44	60

The participants were again divided into two groups, based on the total duration of antipsychotic drug use. Of 29 subjects on antipsychotic drugs for less than one year, 6 were found to have metabolic syndrome. At the same time 10 of 31, who were on antipsychotic drugs for more than 1 year met the criteria for

metabolic syndrome. Chisquare test showed no significant difference with a p value of 0.311.

Correlation of antipsychotic exposure to waist circumference

	N	Pearson correlation coefficient	P value
Waist circumference	60	-0.041	0.756

There was a negative correlation between duration of antipsychotic exposure and waist circumference. However it was not statistically significant.

Correlation of antipsychotic exposure to systolic BP

	N	Pearson correlation coefficient	P value
Systolic BP	60	0.118	0.369

There was a positive correlation between duration of antipsychotic exposure and systolic blood pressure. However it was not statistically significant.

Correlation of antipsychotic exposure to diastolic BP

	N	Pearson correlation coefficient	P value
Diastolic BP	60	0.219	.0.092

There was a positive correlation between duration of antipsychotic exposure and diastolic blood pressure. However it was not statistically significant.

Correlation of antipsychotic exposure to fasting blood sugar

	N	Pearson correlation coefficient	P value
AC	60	0.057	0.666

There was a positive correlation between duration of antipsychotic exposure and fasting blood sugar. However it was not statistically significant.

Correlation of antipsychotic exposure to HDL cholesterol

	N	Pearson correlation coefficient	P value
HDL	60	-0.057	0.666

There was a negative correlation between duration of antipsychotic exposure and HDL cholesterol. However it was not statistically significant.

Correlation of antipsychotic exposure to Triglyceride

	N	Pearson correlation coefficient	p value
TG	60	0.066	0.617

There was a positive correlation between duration of antipsychotic exposure and triglyceride. However it was not statistically significant.

Correlation of duration of Illness to waist circumference

	N	Pearson correlation coefficient	P value
Waist circumference	60	-0.246	0.059

There was a negative correlation between duration of illness and waist circumference. However it was not statistically significant

Correlation of duration of illness to HDL cholesterol

	N	Pearson correlation coefficient	p value
HDL	60	0.054	0.681

There was a positive correlation between duration of illness and waist HDL cholesterol. However it was not statistically significant.

Correlation of duration of illness to Triglyceride serum

	N	Pearson correlation coefficient	P value
Triglyceride	60	0.008	0.954

There was a positive correlation between duration of illness and triglyceride serum. However it was not statistically significant.

Correlation of duration of illness to systolic BP

	N	Pearson correlation coefficient	P value
Systolic BP	60	0.010	0.940

There was a positive correlation between duration of illness and systolic blood pressure. However it was not statistically significant.

Correlation of duration of illness to diastolic BP

	N	Pearson correlation coefficient	P value
Diastolic BP	60	0.088	0.504

There was a positive correlation between duration of illness and diastolic blood pressure. However it was not statistically significant.

Distribution of metabolic syndrome based on age group

Age group	MetS+	No MetS	Total
Less than 40 years	9 (23%)	31(77%)	40
More than 40 years	7(35%)	13(65%)	20
Total	16	36	60

Chisquare value- 1.065 p value- 0.360

Above 40 years of age (35%) had a higher prevalence of metabolic syndrome compared to below 40 years of age (23%). The difference was statistically not significant

Presence of at least 2 criteria out of 5 based on age group

Age group	MetS+	No metS	Total
Less than 40 years	19 (48%)	21(52%)	40
More than 40 years	9(45%)	11 (55%)	20
Total	28(53%)	32(47%)	60

Chisquare value- 0.033 p value - 0.537

The prevalence of at least 2 components of metabolic syndrome was higher in those 40 years of age or below (48%) compared to above 40 years of age (45%). The difference was statistically not significant.

Prevalence of atleast one criteria among 5 based on age group

Age group	MetS+	No metS	Total
Less than 40 years	35 (87%)	5(13%)	40
More than 40 years	16(80%0	4(20%)	20
Total	51(85%)	9(15%)	60

Chisquare value- 0.588 P value - 0.464

The prevalence of at least one component of metabolic syndrome was higher in above 40 years of age(87%) compared to below 40 years of age(80%). The difference was statistically not significant.

DISCUSSION

Out of the total participants recruited, 58% were male and 42 % were female. The Indian census data 2011 shows that the sex ratio is 940 females per 1000 males. The data is reflective of the general population trend in our country. According to Indian census data 2011, 74% percent of the population was literate. In our study 79% percent of the population was found to be literate. This finding is similar to the trend in general population.

In earlier studies the prevalence of metabolic syndrome in mentally ill patients on antipsychotic medication varies from 24 % to 32% (60–62)
In our study the overall prevalence of metabolic syndrome 23 % (IDF) and 27% (NCEP) has shown that the prevalence of metabolic syndrome was high and similar to the earlier studies undertaken. NCEP ATP and IDF have similar criteria for metabolic syndrome and take into account the role of abdominal obesity as a major factor. Our study has yielded a similar percentage of metabolic syndrome using both the criteria.

Some studies have shown that the prevalence of metabolic syndrome in the general population itself is as high as 25 to 30 % (63). Such studies have used the same criteria to diagnose the metabolic syndrome. Lack of physical exercise, nutritional factors, lifestyle factors and genetic vulnerability are proposed to be the major cause of this high prevalence.

The mean age of the participants were found to be 36 in our study. This could be due to the fact that schizophrenia is a condition which starts early in life and most often is a lifelong condition. The fact that the prevalence of metabolic syndrome is slightly low compared to some other studies(62) could be due to the fact that the mean age of our population was 36, which is a younger population. Other reasons may be that patients were better informed and encouraged to follow some physical activities by the treating doctors in this centre where the study was conducted. Further studies may be undertaken in this regard to know the awareness among patients and relatives regarding metabolic abnormalities and importance of diet and exercises.

The gender specific prevalence of metabolic syndrome was calculated according to the NCEP criteria, was found to be higher in females compared to males. Earlier studies have shown an equal prevalence of metabolic syndrome in males and females(60). However some Indian studies have shown higher prevalence of metabolic syndrome in females(63,64).The higher prevalence in females could be due to genetic factors as demonstrated in an earlier study(65).

Correlation between duration of antipsychotic use and metabolic syndrome

The chance of developing metabolic syndrome is higher when the duration of the antipsychotic use increases(60). In our study we found that the prevalence of metabolic syndrome is higher in group of patients taking medication more than one year as compared to patients taking medications for less than a year. The exposure to antipsychotic is an important determining factor for the development of metabolic syndrome. The longer the duration of

antipsychotic use, the more is the chance of developing metabolic syndrome. It could be due to the irreversible metabolic changes due to antipsychotic drugs.

Correlation between duration of illness and metabolic syndrome

The prevalence was higher among patients having illness more than one year. This could be due to fact that such patients are more likely to have been taking medication for a longer duration of time. The disease related factors like genetic factors, sedentary life style, and nutritional factors also would have contributed to the development of metabolic syndrome over a period of time. The effect of lifestyle factors would be more pronounced in this case compared to the genetic vulnerability as both the groups are equally vulnerable. A further study with a prospective design would help to clearly find out the causative effect of duration of mental illness and metabolic syndrome.

There was no earlier study that looked at the relationship between duration of mental illness and risk of metabolic syndrome.

Distribution of individual components of metabolic syndrome

Abnormal HDL cholesterol was present in maximum number of participants 37(62%) followed by increased waist circumference 33(55%), raised triglycerides 25(42%), raised blood pressure 15(25%) or impaired fasting glucose 8 (13%). It is different from a western study which has found blood pressure(38%), HDL (36%) and triglycerides (33%) being the most common components contributing metabolic syndrome (64) . The difference could be due to the ethnic and genetic differences whereby Indians might be more prone to develop central obesity and

lipid abnormalities than hypertension and elevated blood glucose. This suggests that criteria sets using waist circumference to detect metabolic syndrome may be more valid in the Indian population.

Gender wise correlation of individual components of metabolic syndrome

Mean value HDL cholesterol was found to be significantly lower in males compared to females. HDL cholesterol is protective against cardiovascular complications and atherogenesis. It was similar to a study done in the past(64) . This difference could possibly be due to disparity in genetic factors between the genders.

The mean value of waist circumference, triglycerides, and blood pressure were higher among males compared to females. At the same time mean value of fasting blood sugar was higher in females. However the chisquare test did not yield a significant difference between these variables. Studies in the past have showed significant difference in the mean values of these components between the gender (64). Our sample size may have had insufficient power to find a significant difference between these variables, in this study.

Prevalence of atleast two and at least one component of metabolic syndrome.

32 (53%) participants had at least two components of metabolic syndrome and 51(85%) participants had at least one component of the metabolic syndrome.

Females (52%) had higher prevalence of at least two components compared to males (43%). The prevalence of at least one component of metabolic syndrome was higher in females88%) ascompared to males(82%).

However these differences were not statistically significant. The implication of this finding is that the prevalence of individual components of metabolic syndrome is alarmingly high in our study population and risk of complications due to these could also be high. There were no studies in the past which has looked into the prevalence based on the above criteria.

Correlation of duration of antipsychotic exposure and individual components of metabolic syndrome.

There was a positive correlation with triglycerides, blood pressure and fasting blood sugar to duration of antipsychotic exposure. And there was a negative correlation with duration of exposure of antipsychotic to HDL cholesterol. However these correlations were not significant statistically. Earlier studies have shown a positive correlation between duration of antipsychotic exposure and metabolic parameters(66). These finding suggest an increase in the risk of derangement of metabolic parameters as duration of antipsychotic drug increases. A larger sample size may be required to assess this association accurately.

Distribution of metabolic syndrome parameters based on age

The prevalence of metabolic syndrome was higher in age group of 40 years and above (35%) compared to age group below 40 years (23%). These differences were not statistically significant. However, this trend is similar to earlier studies

that have shown an increase in the prevalence of metabolic syndrome as age increases(67,68).

Strengths of the study

1. The main outcome of the study, prevalence of the metabolic syndrome, was calculated using both International Diabetic Federation and National Cholesterol Education Program criteria.
2. Sample of patients selected were from those attending a regular psychiatric clinic, reflecting clinical practice in the real world rather than a selected research sample. This would improve generalizability.

Limitations of the study

1. Sample size was not achieved.
2. Results displayed trends similar to previously done studies, but did not achieve statistical significance.
3. The association between the dose of the drug and the metabolic syndrome could not be calculated. Although the information about drugs and doses were recorded, the lack of medication equivalence figures meant that it could not be translated to an analyzable data.

Clinical implications

The study has found that metabolic syndrome is present in a significant proportion of patients receiving antipsychotic medication at a psychiatric clinic in South India.

Clinicians must be aware of the implications regarding the medication choice and the need to take steps to prevent the development of metabolic syndrome in their patients.

The study also has shown a relation between the duration of antipsychotic medication and metabolic syndrome. This has implications about the choice of drug since several major mental illnesses require long term antipsychotic use.

A higher prevalence of metabolic syndrome in females means that this subgroup is more vulnerable to this major complication.

It is important to provide patients with information regarding the metabolic syndrome and encourage them to do regular physical activity and appropriate diet modifications, particularly as a preventive step.

Equally important is to identify patients who are more vulnerable to develop metabolic syndrome by going through family history and current metabolic status. Before starting antipsychotic medications, it is important to record the baseline anthropometric data and the laboratory parameters. This would help clinicians to identify those more vulnerable to developing metabolic syndrome. It is also important to regularly monitor the patients to see if they develop any features of metabolic syndrome, by regular physical and laboratory examination.

Waist circumference measurement is a simple, inexpensive and sensitive measure of risk for metabolic syndrome.

Future directions

Larger sample size studies would provide more robust data to support these findings. Prospective studies using a cohort of drug naïve patients would provide incidence data. Interventional studies would provide information on the best package of management to treat and prevent development of metabolic syndrome.

This study of metabolic syndrome in those receiving antipsychotics shows that large proportions of such patients have deranged physiological functions, with a significant subset having a full blown metabolic syndrome. Several have sub syndromal conditions. The prevalence matches rates in other studies done. This is a clinically relevant finding emphasizing the need for Indian psychiatrists to be aware of this side effect and to take preventive action while prescribing antipsychotics.

SUMMARY

Introduction

Metabolic syndrome is a group of risk factors when present in an individual, increases the risk of stroke, coronary artery disease and type2 diabetes. There is an increased prevalence of metabolic syndrome in mentally ill patients, due to sedentary life style factors, medication and genetic causes.

An extensive literature review has found a paucity of literature on Indian studies on the prevalence of metabolic syndrome in mentally ill patients.

Methodology

A cross sectional study was done to measure the prevalence of metabolic syndrome in patients using antipsychotic medication. Participants, fulfilling the inclusion and exclusion criteria, were recruited from the outpatient facility in the department of Psychiatry, Christian Medical College, Vellore, after obtaining written informed consent. Socio demographic data, anthropometric variables, fasting blood glucose, HDL cholesterol and serum triglyceride values were measured.

Results

Analysis was done using 60 participants, prevalence of metabolic syndrome was found to be 23%(IDF) and 26%(NCEP). Gender specific prevalence was also calculated, with a prevalence of 20% in males and 36% in females. There was no significant difference in the prevalence of metabolic syndrome in males and

females(p value=0.167). The prevalence of metabolic syndrome was higher in patients receiving antipsychotic medication for more than 1 year (p value= 0.311). Similarly patients having more than one year duration of illness had a higher prevalence of metabolic syndrome(p value= 0.481). The individual components of metabolic syndrome also had a higher prevalence in females, however the differences were not statistically significant except abnormality in HDL cholesterol, which was statistically significant(p value 0.01)

Conclusion

The prevalence of metabolic syndrome was found to be high and was comparable to the earlier studies. The need has arisen for the clinicians to be more cautious while prescribing antipsychotic drugs, anticipate possible development of metabolic syndrome, and take necessary steps to prevent the emergence of this dreaded complication.

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APPENDIX 1

Participant Information Sheet

"Prevalence of metabolic syndrome in patients receiving antipsychotic medication"

My name is Dr. Ranjith P and I am doing a research on a condition called metabolic syndrome. The research will be done in the Department of Psychiatry, CMC, Vellore.

Medications can cause various side effects and antipsychotic drugs which you are receiving may result weight gain, rise in blood sugar, blood pressure and cholesterol.

I am aiming to find out these by checking your weight, height and testing your blood. I would like to request you to donate 10 ml (2 teaspoonfuls) of blood for use in my study. I will also be collecting information regarding your illness from the case record kept in the hospital.

The blood will be taken using sterile (clean) methods by a trained technician. Your information will not be revealed to anyone and all information about you and your treatment will be kept confidential.

You have every right to refuse to take part in this study. Your treatment will not be affected by this.

APPENDIX 2

Consent Form

“Prevalence of metabolic syndrome in patients receiving antipsychotic medication”

I.....residing in.....

.....give consent to take part in a study that looks at presence of raised blood sugars, cholesterol, blood pressure and weight in patients receiving antipsychotic medication. The research has been explained to me in the language known to me. I was given the chance to ask questions about the study . I have received an information sheet as well in my regional language.

My treatment will be the same whether I take part in the study or not . There is no direct benefit to me because of this study. I will not receive any money or gift for taking part in the study other than the travel expenses. My personal details will not be disclosed to anyone .I have no objection for the study results being published in a scientific journal .I can withdraw from the study at any point of this research.

Date: Signature of the participant/Thumb impression

Name of the participant

APPENDIX 3

Participant Information Sheet - Tamil

பிணியாளர் தகவல் படிவம்
"மிகு மனநோய் எதிர்ப்பு மருந்துகள் பெறும் பிணியாளர்களில் ஊன்மச் செயல்பாட்டு நோய்க்குறித் தொகுதியின் பரவு விகிதம்"

என் பெயர் மரு. பி. ரஞ்சித். ஊன்மச் செயல்பட்டு நோய்க்குறித் தொகுதி என்பது
பற்றி நான் ஆய்வு செய்து வருகிறேன். இந்த ஆய்வு வேலூர் சி.எம்.சி. மனநல
மருத்துவத் துறையில் செய்யப்படும்.
மருந்துகளால் பல்வேறு பக்க விளைவுகள் வரலாம். நீங்கள் எடுத்து வரும் மிகு
மனநோய் மருந்துகளால் உடல் எடை, இரத்தச் சர்க்கரை அளவு, இரத்தக்
கொழுப்பு அளவு, இரத்த அழுத்தம் ஆகியவற்றில் அதிகரிப்பு ஏற்படலாம்.
உங்கள் எடை, உயரம், இரத்தம் ஆகியவற்றைப் பரிசோதிப்பதன் மூளலாம் நான்
இதைக் கண்டறிய விரும்புகிறேன். என் ஆய்வுக்காக 10 மிலி (2 தேக்கரண்டி)
இரத்தம் தருமாறு உங்களைக் கேட்டுக்கொள்கிறேன். உங்கள் நோய் பற்றிய
விவரங்களையும் நான் மருத்துவ மனையில் உள்ள பதிவேடுகளில் இருந்து நான்
சேகரித்துக் கொள்வேன்.
பயிற்சி பெற்ற ஒரு பணியாளர் உங்கள் இரத்தத்தைச் சேகரிப்பார். உங்களைப்
பற்றிய தகவல் யாருக்கும் வெளியிடப்பட மாட்டாது. உங்கள் மருத்துவ விவரம்
இரகசியமாக வைக்கப்படும். இந்த பரிசோதனைகள் இலவசமாகச் செய்யப்படும்.
இதற்காக மருத்துவ மனைக்கு வர ஆகும் செலவு உங்களுக்குத் தரப்படும். இந்த
ஆய்வினால் உங்களுக்கு நேரட்டிப் பயன் இருக்கும் வாய்ப்பு இல்லை.
இந்த ஆய்வில் பங்கேற்க மறுக்க உங்களுக்கு எல்லா உரிமையும் உண்டு. அதனால்
உங்கள் மருத்துவம் பாதிக்கப்படாது.
உங்களுக்கு ஏதாவது ஐயம் இருந்தால் வேலூர் சி.எம்.சி. மனநல மருத்துவத் துறை,
தொலைபேசி எண் 04162284520 இல் என்னிடம் தொடர்பு கொள்ளலாம்.
மின்னஞ்சல்: ranjithpadoli@gmail.com

APPENDIX 4
Consent form- Tamil

இசைவுப் படிவம்

"மிகு மனநோய் எதிர்ப்பு மருந்துகள் பெறும் பிணியாளர்களில் ஊன்மச் செயல்பாட்டு நோய்க்குறித் தொகுதியின் பரவுவிகிதம்

.....

என்னும் முகவரியில் வசித்து வரும்
.....
என்னும் நான் மிகு மனநோய் எதிர்ப்பு மருந்துகளைப் பெறும் பிணியாளர்களில் இரத்தச் சர்க்கரை அளவு, இரத்தக் கொழுப்பு அளவு, இரத்த அழுத்தம், உடல் எடை ஆகியவற்றில் அதிகரிப்பு பற்றிய ஓர் ஆய்வில் பங்கேற்குமாறு மரு. ரஞ்சித்தால் கேட்டுக் கொள்ளப்பட்டுள்ளேன். இந்த ஆராய்ச்சி பற்றி நான் அறிந்த மொழியில் எனக்கு விளக்கியுள்ளார்கள். இந்த ஆய்வு பற்றிக் கேள்விகள் கேட்க எனக்கு வாய்ப்பு அளிக்கப்பட்டது. நான் அறிந்த மொழியில் இது பற்றிய ஒரு தகவல் அறிக்கையையும் நான் பெற்றுக் கொண்டுள்ளேன்.

இந்த ஆய்வில் நான் பங்கெடுத்துக் கொண்டாலும் கொள்ளாவிட்டாலும் எனக்குக் கிடைக்கும் மருத்துவம் ஒன்றாகவே இருக்கும். இந்த ஆய்வினால் எனக்கு நேரடிப் பயன் எதுவும் இல்லை. இந்த ஆய்வில் பங்கு பெறுவதற்குப் பயணச் செலவு தவிர வேறு பணமோ பரிசோ எனக்குக் கிடைக்காது. என் சொந்த விவரங்கள் யாருக்கும் வெளியிடப்பட மாட்டா. இந்த ஆய்வின் முடிவுகளை ஓர் அறிவியல் இதழில் வெளியிட எனக்கு எந்தத் தடையும் இல்லை. நான் இந்த ஆய்விலிருந்து எந்த கட்டத்தில் வேண்டுமானாலும் வெளியேறலாம்.

தேதி:

பிணியாளர் கையொப்பம்

பிணியாளர் பெயர்

Introduction

Metabolic syndrome is a constellation of risk factors that when present in an individual, increases the risk for stroke, coronary artery disease and type2 diabetes mellitus. Metabolic syndrome constitutes central obesity, elevated cholesterol and triglycerides, impaired glucose tolerance and high blood pressure. Presence of metabolic syndrome in an individual leads to increased morbidity and mortality.

Patients with schizophrenia and other mental illnesses are especially prone to develop metabolic syndrome, due to their life style factors, genetic predisposition and due to antipsychotic medication. The role of antipsychotic medication in producing

INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE
VELLORE 632 002, INDIA

Dr.B.J.Prashantham, M.A.,M.A.,Dr.Min(Clinical)
Director, Christian Counseling Centre
Editor, Indian Journal of Psychological Counseling
Chairperson, Ethics Committee, IRB

Dr. Alfred Job Daniel, MS Ortho
Chairperson, Research Committee &
Principal

Dr. Nihal Thomas
MD, MNAMS, DNB(Endo), FRACP(Endo), FRCP(Edin)
Secretary, Ethics Committee, IRB
Additional Vice Principal (Research)

18th May, 2012

Dr. Ranjith P
PG Registrar
Department of Psychiatry
Christian Medical College
Vellore 632 002

Sub: **FLUID Research grant project NEW PROPOSAL:**
The prevalence of metabolic syndrome in patients receiving antipsychotic medication.
Dr. Ranjith P, PG Registrar, Psychiatry, Dr. Deepa Braganza, Psychiatry

Ref: IRB Min. No. 7782 dated 9.3.2012

Dear Dr. Ranjith,

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project entitled "The prevalence of metabolic syndrome in patients receiving antipsychotic medication " on March 9, 2012.

The Committees reviewed the following documents:

1. Format for application to IRB submission
2. Consent Form and Information (English and Tamil)
3. Proforma
4. Cv of Dr. Ranjith
5. A CD containing documents 1 - 4

The following Institutional Review Board (Ethics Committee) members were present at the meeting held on March 9, 2012 in the CREST/SACN Conference Room, Christian Medical College, Bagayam, Vellore- 632002.

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CHRISTIAN MEDICAL COLLEGE
VELLORE 632 002, INDIA

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Secretary, Ethics Committee, IRB
Additional Vice Principal (Research)

Name	Qualification	Designation	Other Affiliations
Dr. B.J.Prashantham	MA (Counseling), MA (Theology), Dr Min(Clinical)	Chairperson(IRB)& Director, Christian Counselling Centre	Non-CMC
Mr. Harikrishnan	BL	Lawyer	Non-CMC
Mrs. S. Pattabiraman	BSc, DSSA	Social Worker, Vellore	Non-CMC
Mrs. Ellen Ebenezer Benjamin	M.Sc. (Nursing), Ph.D.	Deputy Nursing Superintendent, CMC.	
Dr. Vathsala Sadan	M.Sc, Ph.D	Addl. Deputy Dean, College Nursing, CMC.	
Dr. Jayaprakash Muliyil	BSC, MBBS, MD, MPH, DrPH(Epid), DMHC	Academic Officer, CMC	
Mr. Joseph Devaraj	BSc, BD	Chaplain, CMC	
Dr. Nihal Thomas	MD MNAMS DNB(Endo) FRACP(Endo) FRCP(Edin)	Secretary IRB (EC)& Dy. Chairperson (IRB), Professor of Endocrinology & Addl. Vice Principal (Research), CMC.	

We approve the project to be conducted as presented.

The Institutional Ethics Committee expects to be informed about the progress of the project, any serious adverse events occurring in the course of the project, any changes in the protocol and the patient information/informed consent and requires a copy of the final report.

A sum of Rs 20,000/- (Rupees Twenty thousand only) will be sanctioned for 6 months after receipt of the revised proposal.

Yours sincerely,

Dr. Nihal Thomas
Secretary (Ethics Committee)
Institutional Review Board

Secretary
Institutional Review Board
(Ethics Committee)
Christian Medical College
Vellore - 632 002, Tamil Nadu, India

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1	id	nmae	age	Mar sts	emplo	sex	edu	dia	duri	dura	apdd	waist	bps	bpd	ac	hdl	tg	
2	1	KR	42	2	2	2	3	1	4	3		90	110	80	101	29	237	
3	2	RL	27	1	1	1	5	1	24	8		101	110	70	87	45	151	
4	3	TH	34	2	1	2	3	1	14	12		68	100	70	79	43	135	
5	4	MM	25	1	1	1	3	1	10	7		78	110	70	88	35	176	
6	5	NK	23	1	1	1	6	1	14	13		101	120	70	97	37	84	
7	6	PL	29	2	2	1	2	1	8	8		87	124	80	92	29	171	
8	7	JD	36	2	1	2	2	1	4	4		78	100	70	71	36	91	
9	8	SM	22	2	1	1	6	1	5	5		93	120	80	79	42	106	
10	9	ML	34	2	1	2	2	1	48	40		92	100	70	95	36	154	
11	10	DL	24	1	1	1	4	1	42	4		84	130	70	79	36	155	
12	11	RI	45	2	1	2	4	1	72	42		96	130	70	83	46	87	
13	12	DR	37	1	1	1	7	1	60	6		84	130	80	85	36	179	
14	13	GI	34	3	1	2	3	1	144	72		83	100	70	83	46	177	
15	14	PL	35	2	2	1	2	1	120	30		77	120	70	90	45	62	
16	15	MP	40	2	1	2	3	1	5	5		88	120	80	125	61	353	
17	16	GS	41	2	2	1	5	1	144	36		75	120	80	91	35	97	
18	17	BI	25	2	1	2	3	1	72	66		92	120	80	100	30	256	
19	18	PE	32	1	2	1	4	1	30	6		86	134	80	88	42	173	
20	19	KL	55	3	1	2	2	1	84	24		68	110	70	85	73	201	
21	20	DK	25	1	1	1	6	1	24	6		74	100	80	93	26	186	
22	21	KL	43	2	1	2	1	1	24	18		86	110	70	95	39	113	
23	22	DB	30	1	2	1	3	1	60	36		105	116	80	98	41	70	
24	23	JA	27	1	1	1	2	1	24	20		107	120	84	108	38	105	
25	24	KL	55	3	1	2	1	1	84	42		85	110	70	88	38	139	
26	25	VY	53	2	1	2	2	1	120	108		105	130	80	114	32	225	
27	26	AP	65	2	1	2	2	1	30	6		77	120	80	84	37	161	
28	27	SN	35	2	1	1	1	1	144	96		80	130	80	83	38	188	
29	28	NL	38	2	1	2	2	1	11	10		88	110	70	85	51	63	
30	29	MY	60	2	1	1	1	1	192	120		85	150	90	105	36	336	
31	30	MH	31	1	1	1	1	1	96	6		97	120	80	93	42	333	

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32	31	PR	25	1	1	1	3	1	12	10		77	110	70	81	38	98	
33	32	AS	28	1	1	1	6	1	120	5		72	110	70	83	42	76	
34	33	SL	48	2	1	1	3	1	240	180		76	110	70	96	55	57	
35	34	SA	37	2	1	1	1	1	76	5		74	120	84	88	39	89	
36	35	SR	32	2	1	1	3	1	252	240		78	100	70	91	36	176	
37	36	KK	27	1	1	1	2	1	120	7		78	100	70	81	34	97	
38	37	JM	20	2	1	2	3	1	5	5		86	110	70	82	54	61	
39	38	SH	28	1	1	1	6	1	60	42		112	130	80	84	33	164	
40	39	RA	28	1	1	1	1	4	24	3		105	120	82	85	50	88	
41	40	SR	26	1	1	1	2	1	39	36		97	140	86	88	35	117	
42	41	MN	24	1	1	1	3	1	18	12		79	130	80	88	31	108	
43	42	PY	48	1	1	1	1	1	12	9		96	120	80	91	42	155	
44	43	PA	50	2	1	2	3	1	36	18		80	114	70	93	58	75	
45	44	RJ	53	1	1	2	3	1	30	24		91	110	70	95	32	274	
46	45	SJ	43	2	1	2	2	1	60	12		93	120	80	108	41	212	
47	46	PL	29	1	2	1	2	1	24	12		85	120	78	94	31	70	
48	47	JC	38	1	1	1	1	1	180	132		78	110	70	94	31	134	
49	48	KS	39	2	1	1	2	1	120	120		94	120	70	95	33	146	
50	49	NM	24	3	1	2	1	1	18	4		77	120	80	92	47	41	
51	50	JB	55	3	1	2	3	1	96	84		90	140	86	91	50	60	
52	51	SM	24	2	1	2	2	1	96	17		103	110	70	89	46	76	
53	52	RH	28	1	1	1	1	1	144	48		65	120	80	93	43	56	
54	53	KL	55	3	1	2	1	1	96	36		86	120	80	96	73	121	
55	54	GI	28	1	1	2	1	1	72	24		100	130	80	185	50	96	
56	55	SI	37	2	1	2	1	1	96	48		84	140	88	83	54	111	
57	56	VC	24	2	1	1	1	1	24	3		88	130	80	94	35	277	
58	57	E	39	2	1	1	1	1	24	24		92	136	80	81	33	535	
59	58	GM	42	2	2	1	1	1	10	8		82	126	80	90	45	84	
60	59	KL	50	2	1	2	1	1	36	5		94	110	70	89	50	39	
61	60	IB	43	1	1	1	1	1	30	24		108	120	70	71	44	76	
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